

48,XXYY syndrome

Description

48,XXYY syndrome is a chromosomal condition that causes an inability to have children (infertility), developmental and behavioral disorders, and other health problems.

48,XXYY disrupts sexual development, though affected individuals are typically assigned male gender at birth. Adolescents and adults with this condition usually have small testes that do not produce enough testosterone, which is the hormone that directs male sexual development. A shortage of testosterone during puberty can lead to reduced facial and body hair, poor muscle development, low energy levels, and an increased risk of breast enlargement (gynecomastia). Because their testes do not function normally, individuals with 48,XXYY syndrome are infertile.

48,XXYY syndrome can affect other parts of the body as well. Affected individuals are often taller than their peers with an average adult height of 6 feet 4 inches (193 cm). They tend to develop a tremor that typically starts in adolescence and increases with age. Dental problems are frequently seen with this condition and include delayed appearance of the primary (baby) or secondary (adult) teeth, thin tooth enamel, crowded or misaligned teeth, and multiple cavities.

As people with 48,XXYY get older, they may develop a narrowing of the blood vessels in the legs, called peripheral vascular disease. Peripheral vascular disease can cause skin ulcers to form. Affected individuals are also at risk of developing a type of clot called a deep vein thrombosis (DVT) that occurs in the deep veins of the legs. Additionally, individuals with 48,XXYY syndrome may have flat feet (pes planus), elbow abnormalities, abnormal fusion of certain bones in the forearm (radioulnar synostosis), allergies, asthma, type 2 diabetes, seizures, and congenital heart defects.

Most individuals with 48,XXYY syndrome have an IQ that ranges from 70-80 and some degree of difficulty with speech and language development. Some children with 48,XXYY syndrome have delayed development of motor skills such as sitting, standing, and walking that can lead to poor coordination. Learning disabilities, especially those that are language-based, are very common in this disorder. People with 48,XXYY seem to perform better at tasks focused on math, visual-spatial skills such as puzzles, and memorization of locations or directions. Affected individuals have higher than average rates of behavioral disorders, such as attention-deficit/hyperactivity disorder (ADHD); mood disorders, including anxiety and bipolar disorder; and autism spectrum disorder, which affects communication and social interaction.

Frequency

48,XXYY syndrome is estimated to affect 1 in 18,000 to 40,000 male newborns.

Causes

48,XXYY syndrome is a condition related to the X and Y chromosomes (the sex chromosomes). People normally have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Females typically have two X chromosomes (46,XX), and males have one X chromosome and one Y chromosome (46,XY). 48,XXYY syndrome results from the presence of an extra copy of both sex chromosomes in each of a male's cells (48,XXYY). Extra copies of genes on the X chromosome interfere with sexual development, preventing the testes from functioning normally and reducing the levels of testosterone. Many genes are found only on the X or Y chromosome, but genes in areas known as the pseudoautosomal regions are present on both sex chromosomes. Extra copies of genes from the pseudoautosomal regions of the extra X and Y chromosome contribute to the signs and symptoms of 48,XXYY syndrome; however, the specific genes have not been identified.

[Learn more about the chromosomes associated with 48,XXYY syndrome](#)

- x chromosome
- y chromosome

Inheritance

48,XXYY is not inherited; it usually occurs as a random event during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in a reproductive cell with an abnormal number of chromosomes. In 48,XXYY syndrome, the extra sex chromosomes almost always come from a sperm cell. Nondisjunction may cause a sperm cell to gain two extra sex chromosomes, resulting in a sperm cell with three sex chromosomes (one X and two Y chromosomes). If that sperm cell fertilizes a normal egg cell with one X chromosome, the resulting child will have two X chromosomes and two Y chromosomes in each of the body's cells.

In a small percentage of cases, 48,XXYY syndrome results from nondisjunction of the sex chromosomes in a 46,XY embryo very soon after fertilization has occurred. This means that a normal sperm cell with one Y chromosome fertilized a normal egg cell with one X chromosome, but right after fertilization nondisjunction of the sex chromosomes caused the embryo to gain two extra sex chromosomes, resulting in a 48,XXYY embryo.

Other Names for This Condition

- XXYY syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Anomaly of sex chromosome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0036868/>)

Genetic and Rare Diseases Information Center

- 48,XXYY syndrome (<https://rarediseases.info.nih.gov/diseases/5677/48xxyy-syndrome>)

Patient Support and Advocacy Resources

- Disease InfoSearch (<https://www.diseaseinfosearch.org/>)
- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (<https://clinicaltrials.gov/ct2/results?cond=%2248%2CXXYY+syndrome%22+OR+%22XXYY%22>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%2848,+XXYY%5BTIAB%5D%29+OR+%28XXYY%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

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